General

Guideline Title

Extragonadal germ cell tumours.

Bibliographic Source(s)

Alberta Provincial Genitourinary Tumour Team. Extragonadal germ cell tumours. Edmonton (Alberta): CancerControl Alberta; 2013 Apr. 8 p. (Clinical practice guideline; no. GU-007). [24 references]

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Diagnosis

- If a patient presents with undifferentiated adenocarcinoma of unknown origin, copy number of chromosome i12p should be performed.
- Lactate dehydrogenase (LDH), alpha fetoprotein (AFP) and gonadotropin (hCG) should be assessed.
- Patients should be classified and treated based on prognosis (International Germ Cell Cancer Collaborative Group [IGCCCG], 1997)

Table. Prognostic Factors for Germ Cell Tumours (GCTs)

Prognosis	Non-seminoma	Seminoma
Good	Primary extragonadal retroperitoneal • and low markers: AFP <1,000 ng/ml • and β-hCG <1,000 ng/ml (<5,000 IU/l) • and LDH <1.5 x normal level • and no non-pulmonary visceral metastases	• Any primary localization • Any marker level • No non-pulmonary visceral metastases
Intermediate	Primary extragonadal retroperitoneal • and AFP 1,000–10,000 ng/ml	• Any primary localization • Presence of non-pulmonary visceral metastases (liver, CNS, bone, intestinum)

Prognosis	Non-seminoma	Seminoma
	• and/or β-hCG 1,000–10,000 ng/ml (5,000-50,000 IU/l) • and/or LDH 1.5–10 x normal level • and no non-pulmonary visceral metastases	• Any marker level

Poor	Primary mediastinal GCT with or without testis or primary retroperitoneal tumour
	• and presence of non-pulmonary visceral metastases (liver, CNS, bone, intestinum)
	• and/or "high markers"
	  • AFP >10,000 ng/ml
	  • β-hCG >10,000 ng/ml (50,000 IU/l)
	• or LDH >10 x normal level
		N/A

AFP, alpha fetoprotein; β-hCG, beta human chorionic gonadotropin; CNS, central nervous system; GCT, germ cell tumour; LDH, lactate dehydrogenase

Management

1. Patients should be considered for clinical trials.
2. Bleomycin, etoposide and cisplatin (BEP) or etoposide, ifosfamide, cisplatin (VIP) is recommended as first-line chemotherapy, with the number of cycles given based on risk category.
3. For failure or relapse on either of these regimens and good risk disease, high dose chemotherapy and peripheral blood stem cell transplantation can be given. Recommended agents for high dose chemotherapy include ifosfamide, vinblastine, carboplatin, etoposide and paclitaxel.
4. Patients who are classified as poor risk at relapse should be considered early for high dose chemotherapy and peripheral blood stem cell transplantation, as they may not be well enough to consider this treatment in the third line setting.
5. Patients with mediastinal germ cell tumours (GCTs) who relapse have poor prognosis. Transplant should not routinely be offered to these patients. However, depending on the results from salvage chemotherapy, patient performance status, individual factors and patient's desire to pursue the transplant, it may be considered only after an honest discussion between the clinician and patient as the chance of long term remission and cure are very low.
6. After the completion of chemotherapy, strong consideration for retroperitoneal lymph node dissection should be given in those patients with retroperitoneal primary GCTs.
7. After the completion of chemotherapy, surgery to resect any residual masses should be strongly considered in those patients with mediastinal primary GCTs.

Table. Suggested Follow-up Schedule for Germ Cell Tumours (British Columbia Cancer Agency, 2005)

Group	Clinical Examination and Diagnostics	Frequency of Exam (Months)					
		Year 1	Year 2	Year 3	Year 4	Year 5	Years 5–10
Good Prognosis	LDH, AFP, hCG, clinical exam	3	3	3	3	3	6
	X-ray of the chest or CT scan of chest (if supradiaph. disease)	3–6*	4	6	6	6	
	CT scan of the abdomen/pelvis	3	4	6	6	6	
Intermediate and Poor Prognosis	LDH, AFP, hCG, clinical exam	3	3	3	3	3	6
	X-ray of the chest or CT scan of chest (if supradiaph. disease)	3–6*	3–6*	4–6*	6	6	
	CT scan of the abdomen/pelvis	3	3	4	6	6	

AFP, alpha fetoprotein; hCG, human chorionic gonadotropin; CT, computed tomography; LDH, lactate dehydrogenase

*Depending on the presence of intrathoracic disease.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Extragonadal germ cell tumours (GCTs)

Guideline Category

Diagnosis

Evaluation

Management

Treatment

Clinical Specialty

Oncology

Surgery

Urology

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To provide guidance on appropriate management strategies for patients with primary mediastinal or retroperitoneal germ cell tumours (GCTs)

Target Population

Postpubertal patients with primary mediastinal or retroperitoneal germ cell tumours (GCTs)

Interventions and Practices Considered

Diagnosis/Evaluation

1. Obtaining copy number of chromosome i12p in patients with undifferentiated adenocarcinoma of unknown origin
2. Laboratory testing: lactate dehydrogenase (LDH), alpha fetoprotein (AFP) and gonadotropin (hCG)
3. Classification and treatment of patients based on prognosis

Treatment/Management

1. Consideration for clinical trials
2. Bleomycin, etoposide and cisplatin (BEP) or etoposide, ifosfamide, cisplatin (VIP) as first-line chemotherapy
3. High-dose chemotherapy (e.g., ifosfamide, vinblastine, carboplatin, etoposide and paclitaxel) and peripheral blood stem cell transplantation for treatment failure or relapse
4. Retroperitoneal lymph node dissection in patients with retroperitoneal primary germ cell tumours (GCTs)
5. Surgery to resect residual masses
6. Follow-up examinations based on prognosis

Major Outcomes Considered

- Survival rate (2-year, 5-year, overall, progression-free)
- Remission rate
- Treatment-related toxicity
- Surgical complications, including intra-operative deaths

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Research Questions

Specific research questions to be addressed by the guideline document were formulated by the guideline lead(s) and Knowledge Management (KM) Specialist using the PICO question format (patient or population, intervention, comparisons, outcomes).

Guideline Question

What are the appropriate management strategies for patients with primary mediastinal or retroperitoneal germ cell tumours (GCTs)?

Search Strategy

The PubMed database was searched using the terms (retroperitoneal OR mediastinal) AND germ cell AND primary, published between 1946 and 2012 April. Results were limited to clinical trials, studies in humans, meta-analyses, and practice guidelines. The Medline database was then searched for relevant literature using the MeSH terms "Neoplasm, germ cell and embryonal" with subheadings drug therapy, radiotherapy, therapy, and surgery, combined with "extragonadal." Results were limited to literature published between 1946 and 2012 April. Studies involving fewer than ten patients with extragonadal GCTs, as well as single case studies, were excluded.

Websites of the following guideline developers were searched for relevant guidelines: National Comprehensive Cancer Network (NCCN), British Columbia Cancer Agency (BCCA), European Society of Medical Oncology (ESMO), National Institutes of Health and Care Excellence (NICE), American Society of Clinical Oncology (ASCO), Scottish Intercollegiate Guidelines Network (SIGN), Cancer Council Australia (CCA) and Cancer Care Ontario (CCO).

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Not stated

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Evidence was selected and reviewed by a working group comprised of members from the Alberta Provincial Genitourinary Tumour Team and a Knowledge Management (KM) Specialist from the Guideline Utilization Resource Unit (GURU). A detailed description of the methodology followed during the guideline development process can be found in the Guideline Utilization Resource Unit Handbook (see the "Availability of Companion Documents" field).

Evidence Tables

Evidence tables containing the first author, year of publication, patient group/stage of disease, methodology, and main outcomes of interest are assembled using the studies identified in the literature search. Existing guidelines on the topic are assessed by the KM Specialist using portions of the Appraisal of Guidelines Research and Evaluation (AGREE) II instrument (http://www.agreetrust.org) and those meeting the minimum requirements are included in the evidence document. Due to limited resources, GURU does not regularly employ the use of multiple reviewers to rank the level of evidence; rather, the methodology portion of the evidence table contains the pertinent information required for the reader to judge for himself the quality of the studies.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Formulating Recommendations

The working group members formulated the guideline recommendations based on the evidence synthesized by the Knowledge Management (KM) Specialist during the planning process, blended with expert clinical interpretation of the evidence. As detailed in the Guideline Utilization Resource Unit Handbook (see the "Availability of Companion Documents" field), the working group members may decide to adopt the recommendations of another institution without any revisions, adapt the recommendations of another institution or institutions to better reflect local practices, or develop their own set of recommendations by adapting some, but not all, recommendations from different guidelines.

The degree to which a recommendation is based on expert opinion of the working group and/or the Provincial Tumour Team members is explicitly stated in the guideline recommendations. Similar to the American Society of Clinical Oncology (ASCO) methodology for formulating guideline recommendations, the Guideline Utilization Resource Unit (GURU) does not use formal rating schemes for describing the strength of the recommendations, but rather describes, in conventional and explicit language, the type and quality of the research and existing guidelines that were taken into consideration when formulating the recommendations.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

This guideline was reviewed and endorsed by the Alberta Provincial Genitourinary Tumour Team.

When the draft guideline document has been completed, revised, and reviewed by the Knowledge Management (KM) Specialist and the working group members, it is sent to all members of the Provincial Tumour Team for review and comment. This step ensures that those intended to use the guideline have the opportunity to review the document and identify potential difficulties for implementation before the guideline is finalized. Depending on the size of the document, and the number of people it is sent to for review, a deadline of one to two weeks will usually be given to submit any feedback. Ideally, this review will occur prior to the annual Provincial Tumour Team meeting, and a discussion of the proposed edits will take place at the meeting. The working group members will then make final revisions to the document based on the received feedback, as appropriate. Once the guideline is finalized, it will be officially endorsed by the Provincial Tumour Team Lead and the Executive Director of Provincial Tumour Programs.

Evidence Supporting the Recommendations

References Supporting the Recommendations

British Columbia Cancer Agency. Testis. Cancer management guidelines-genitourinary. Vancouver (BC): British Columbia Cancer Agency; 2005 Jun.

IGCCCG. International Germ Cell Consensus Classification: a prognostic factor-based staging system for metastatic germ cell cancers. International Germ Cell Cancer Collaborative Group. J Clin Oncol. 1997 Feb;15(2):594-603. PubMed

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate diagnosis and management of extragonadal germ cell tumours (GCTs)

Potential Harms

- Adverse effects of chemotherapy, including gastrointestinal, hepatobiliary, genitourinary, and hematologic toxicity
- Researchers reported a 25-year single institution experience of post-chemotherapy surgery for 158 patients with mediastinal primary non-seminoma germ cell tumours (GCTs). Intra-operative deaths occurred in 6% of patients, 90% of which were due to respiratory failure. Post-operative complications occurred in 18% of patients.

Qualifying Statements

Qualifying Statements

The recommendations contained in this guideline are a consensus of the Alberta Provincial Genitourinary Tumour Team and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

Implementation of the Guideline

Description of Implementation Strategy

- Present the guideline at the local and provincial tumour team meetings and weekly rounds.
- Post the guideline on the Alberta Health Services Web site.
- Send an electronic notification of the new guideline to all members of CancerControl Alberta.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Alberta Provincial Genitourinary Tumour Team. Extragonadal germ cell tumours. Edmonton (Alberta): CancerControl Alberta; 2013 Apr. 8 p. (Clinical practice guideline; no. GU-007). [24 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013 Apr

Guideline Developer(s)

CancerControl Alberta - State/Local Government Agency [Non-U.S.]

Source(s) of Funding

CancerControl Alberta

Guideline Committee

Alberta Provincial Genitourinary Tumour Team

Composition of Group That Authored the Guideline

Members of the Alberta Provincial Genitourinary Tumour Team include medical oncologists, radiation oncologists, urologists, pathologists, nurses, and pharmacists.

Financial Disclosures/Conflicts of Interest

Participation of members of the Alberta Provincial Genitourinary Tumour Team in the development of this guideline has been voluntary and the authors have not been remunerated for their contributions. There was no direct industry involvement in the development or dissemination of this guideline. CancerControl Alberta recognizes that although industry support of research, education and other areas is necessary in order to advance patient care, such support may lead to potential conflicts of interest. Some members of the Alberta Provincial Genitourinary Tumour Team are involved in research funded by industry or have other such potential conflicts of interest. However the developers of this guideline are satisfied it was developed in an unbiased manner.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the Alberta Health Services Web site .

Availability of Companion Documents

The following is available:

- Guideline utilization resource unit handbook. Edmonton (Alberta): CancerControl Alberta; 2013 Jan. 5 p. Electronic copies: Available from the Alberta Health Services Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on August 12, 2014. The information was verified by the guideline developer on September 25, 2014.

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